Welcome to STN International! Enter x:x

LOGINID: SSPTAJDA1614

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

```
Web Page for STN Seminar Schedule - N. America
NEWS
NEWS
        AUG 10
                 Time limit for inactive STN sessions doubles to 40
                 minutes
NEWS
     3
        AUG 18
                COMPENDEX indexing changed for the Corporate Source
                 (CS) field
NEWS
        AUG 24
                 ENCOMPLIT/ENCOMPLIT2 reloaded and enhanced
NEWS
        AUG 24
                 CA/CAplus enhanced with legal status information for
                 U.S. patents
NEWS
        SEP 09
                 50 Millionth Unique Chemical Substance Recorded in
                 CAS REGISTRY
                WPIDS, WPINDEX, and WPIX now include Japanese FTERM
NEWS
     7 SEP 11
                 thesaurus
NEWS 8 OCT 21
                Derwent World Patents Index Coverage of Indian and
                 Taiwanese Content Expanded
NEWS 9
        OCT 21 Derwent World Patents Index enhanced with human
                 translated claims for Chinese Applications and
                 Utility Models
NEWS 10 NOV 23 Addition of SCAN format to selected STN databases
NEWS 11
        NOV 23 Annual Reload of IFI Databases
NEWS 12
        DEC 01 FRFULL Content and Search Enhancements
NEWS 13
        DEC 01 DGENE, USGENE, and PCTGEN: new percent identity
                 feature for sorting BLAST answer sets
NEWS 14
        DEC 02
                Derwent World Patent Index: Japanese FI-TERM
                 thesaurus added
NEWS 15
        DEC 02
                PCTGEN enhanced with patent family and legal status
                 display data from INPADOCDB
NEWS 16
        DEC 02 USGENE: Enhanced coverage of bibliographic and
                 sequence information
```

NEWS EXPRESS MAY 26 09 CURRENT WINDOWS VERSION IS V8.4, AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2009.

NEWS HOURS STN Operating Hours Plus Help Desk Availability NEWS LOGIN Welcome Banner and News Items

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN customer agreement. This agreement limits use to scientific research. Use for software development or design, implementation of commercial gateways, or use of CAS and STN data in the building of commercial products is prohibited and may result in loss of user privileges and other penalties.

 => file registry
COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 0.22 0.22

FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 16:47:57 ON 02 DEC 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2009 American Chemical Society (ACS)

Property values tagged with IC are from the  ${\tt ZIC/VINITI}$  data file provided by InfoChem.

STRUCTURE FILE UPDATES: 1 DEC 2009 HIGHEST RN 1194901-26-2 DICTIONARY FILE UPDATES: 1 DEC 2009 HIGHEST RN 1194901-26-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 26, 2009.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> s CHIR 258/cn

L1 1 CHIR 258/CN

=> d 11

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN

RN 692737-80-7 REGISTRY

ED Entered STN: 14 Jun 2004

CN Propanoic acid, 2-hydroxy-, compd. with 4-amino-5-fluoro-3-[6-(4-methyl-1-piperazinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone (1:1) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Propanoic acid, 2-hydroxy-, compd. with 4-amino-5-fluoro-3-[5-(4-methyl-1-piperazinyl)-1H-benzimidazol-2-yl]-2(1H)-quinolinone (1:1) (9CI)

OTHER NAMES:

CN CHIR 258

CN Dovitinib lactate

CN TKI 258

DR 1000873-96-0

MF C21 H21 F N6 O . C3 H6 O3

SR CA

LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL

CM 1

CRN 405169-16-6

CMF C21 H21 F N6 O

CM 2

CRN 50-21-5 CMF C3 H6 O3

$$^{\rm OH}_{\mid}$$
 Me— CH— CO<sub>2</sub>H

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

61 REFERENCES IN FILE CA (1907 TO DATE)

2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

63 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s 405169-16-6/crn L2 31 405169-16-6/CRN

=> d 12

L2 ANSWER 1 OF 31 REGISTRY COPYRIGHT 2009 ACS on STN

RN 1187448-25-4 REGISTRY

ED Entered STN: 06 Oct 2009

CN INDEX NAME NOT YET ASSIGNED

MF C21 H21 F N6 O .  $\times$  C3 H7 N O . C3 H6 O3

SR CA

LC STN Files: CA, CAPLUS

CM 1

CRN 405169-16-6 CMF C21 H21 F N6 O

CRN 68-12-2 CMF C3 H7 N O

CM 3

CRN 50-21-5 CMF C3 H6 O3

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d his

(FILE 'HOME' ENTERED AT 16:47:45 ON 02 DEC 2009)

FILE 'REGISTRY' ENTERED AT 16:47:57 ON 02 DEC 2009

L1 1 S CHIR 258/CN L2 31 S 405169-16-6/CRN

=> file caplus
COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 10.41 10.63

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 16:49:05 ON 02 DEC 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2009 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 2 Dec 2009 VOL 151 ISS 23
FILE LAST UPDATED: 1 Dec 2009 (20091201/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2009
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2009

CAplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2009.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 12

L3 64 L2

=> s 13 and ad<20031107

4775475 AD<20031107 (AD<20031107)

L4 2 L3 AND AD<20031107

=> d 14 1-2 ibib abs

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:1242789 CAPLUS

DOCUMENT NUMBER: 143:477969

TITLE: Preparation of benzimidazole quinolinones for inhibiting FGFR3 and treating multiple myeloma

INVENTOR(S): Cai, Shaopei; Chou, Joyce; Harwood, Eric; Heise, Carla

C.; Machajewski, Timothy D.; Ryckman, David; Shang,

Xiao; Wiesmann, Marion; Zhu, Shuguang

PATENT ASSIGNEE(S): Chiron Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 239 pp., Cont.-in-part of U.S.

Ser. No. 644,055.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 20050261307 US 20040092535 US 7470709	A1 A1 B2	20051124 20040513 20081230	US 2004-983174 US 2003-644055		20041105 20030819 <
CN 1692112 US 20050203101 ZA 2006003598 US 20090281100	A A1 A A1	20051102 20050915 20080430 20091112	CN 2003-824565 US 2004-839793 ZA 2006-3598 US 2008-317493		20030819 < 20040505 20060505 20081223
US 20090181979 PRIORITY APPLN. INFO.:	A1	20090716	US 2009-398130 US 2002-405729P US 2002-426107P US 2002-426226P US 2002-426282P US 2002-428210P US 2003-460327P US 2003-460328P US 2003-460493P US 2003-478916P US 2003-484048P	P P P P P P P	20090304 20020823 20021113 20021113 20021121 20030403 20030403 20030403 20030616 20030701
			US 2003-644055 US 2003-517915P US 2003-526425P US 2003-526426P US 2004-546017P US 2004-982543	A2 P P P P B1	20030819 20031107 20031202 20031202 20040219 20041105

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT

AΒ The title compds. I [A, B, C, and D = C, N; R1-R3 = H, halo, CN, NO2, etc.; R4 = H, alkyl; R5-R8 = H, halo, CN, NO2, etc.; R9 = H, (un) substituted alkyl, aryl, etc.; R10 = H], useful for inhibiting fibroblast growth factor receptor 3 or treating a biol. condition mediated by fibroblast growth factor receptor 3, were prepared E.g., a multi-step synthesis of 4-amino-5-fluoro-3-[6-(4-methylpiperazin-1-yl)-1Hbenzimidazol-2-yl]-1H-quinolin-2-one (II), starting from 5-chloro-2-nitroaniline and 1-methylpiperazine, was given. The majority of the exemplary compds. I displayed an IC50 of less than 10  $\mu M$  with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, Cdk4, MEK1, NEK-2, CHK2, CK1&, Raf, Fyn, Lck, Rsk2, PAR-1, c-Kit, c-ABL, p60src, FGFR3, FLT-3, PDGFR $\alpha$ , and PDGFR $\beta$ . In addition, many of the exemplary compds. exhibited IC50 values in the nM range and show potent activity with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, FGFR3, c-Kit, c-ABL, FLT-3, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, MEK1, CHK2, Fyn, Lck, Rsk2, PAR-1, PDGFR $\alpha$ , and PDGFR $\beta$  with IC50 values of less than 1  $\mu\text{M}$ . The mentioned above compound II was tested in various tests and showed significant antiproliferative activity. II inhibited FGFR3 receptor phosphorylation and ERK phosphorylation in multiple myeloma cell lines with activating FGFR3 mutations.

Ι

ΙI

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:1223876 CAPLUS

DOCUMENT NUMBER: 143:477966

TITLE: Preparation of benzimidazole quinolinones for

inhibiting a checkpoint kinase 1 and their use in

combination therapy for cancer

INVENTOR(S): Gesner, Thomas G.; Barsanti, Paul A.; Harrison,

Stephen D.; Ni, Zhi-Jie; Brammeier, Nathan M.; Zhou,

Yasheen; Le, Vincent P.

PATENT ASSIGNEE(S): Chiron Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 249 pp., Cont.-in-part of U.S.

Ser. No. 644,055.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 20050256157	A1	20051117	US 2005-41191		20050121
US 20040092535	A1	20040513	US 2003-644055		20030819 <
US 7470709	В2	20081230			
CN 1692112	A	20051102	CN 2003-824565		20030819 <
US 20050203101	A1	20050915	US 2004-839793		20040505
US 20090281100	A1	20091112	US 2008-317493		20081223
PRIORITY APPLN. INFO.:			US 2002-405729P	P	20020823
			US 2002-426107P	P	20021113
			US 2002-426226P	P	20021113
			US 2002-426282P	P	20021113
			US 2002-428210P	P	20021121
			US 2003-460327P	P	20030403
			US 2003-460328P	P	20030403
			US 2003-460493P	P	20030403
			US 2003-478916P	P	20030616
			US 2003-484048P	P	20030701
			US 2003-644055	A2	20030819
			US 2004-538984P	P	20040123

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT OTHER SOURCE(S): CASREACT 143:477966; MARPAT 143:477966 GI

The title compds. [I; A, B, C, D = C, N; R1 = H, halo, CN, NO2, etc.; R2, AΒ R3 = H, halo, NO2, CN, etc.; R4 = H, (un)substituted alkyl; R5, R8 = H, (un) substituted alkyl, alkenyl, heterocyclyl; or R5 may be absent if A = N; or R8 may be absent if D = N; R6, R7 = H, halo, NO2, CN, etc.; R9 = H, (un) substituted alkyl, aryl, etc.; R10 = H; or R9 and R10 join together to form one or more rings, each having 5-7 members], useful for inhibiting checkpoint kinase 1, inducing cell cycle progression, and increasing apoptosis in cells, were prepared E.g., a multi-step synthesis of 4-amino-3-(benzimidazol-2-yl)-6-(4-methylpiperazinyl)hydroquinolin-2-one, was given. The compds. I were tested against various kinases. Two of the prepared compds. I, 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1Hbenzimidazol-2-yl)-6-chloroquinolin-2-(1H)-one and 6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-[(piperidin-2-ylmethyl) amino]quinolin-2(1H)-one, were found to be potent inhibitors of CHK1 with IC50 of 0.32 nM and 0.63 nM, resp. The majority of the

exemplary compds. I displayed an IC50 of less than 10  $\mu\text{M}$  with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, Cdk4, MEK1, NEK-2, CHK2, CK1ɛ, Raf, Fyn, Lck, Rsk2, PAR-1, c-Kit, c-ABL, p60src, FGFR3, FLT-3, PDGFR $\alpha$ , and PDGFR $\beta$ . In addition, many of the exemplary compds. exhibited IC50 values in the nM range and show potent activity with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, FGFR3, c-Kit, c-ABL, FLT-3, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, MEK1, CHK2, Fyn, Lck, Rsk2, PAR-1, PDGFR $\alpha$ , and PDGFR $\beta$  with IC50 values of less than 1  $\mu$ M. The compds. I may be used to prepare pharmaceutical compns. and may be used in conjunction with DNA damaging agents. OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS) => d his (FILE 'HOME' ENTERED AT 16:47:45 ON 02 DEC 2009) FILE 'REGISTRY' ENTERED AT 16:47:57 ON 02 DEC 2009 1 S CHIR 258/CN L2 31 S 405169-16-6/CRN FILE 'CAPLUS' ENTERED AT 16:49:05 ON 02 DEC 2009 64 S L2 2 S L3 AND AD<20031107 => d 11YOU HAVE REQUESTED DATA FROM FILE 'REGISTRY' - CONTINUE? (Y)/N:y ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN L1692737-80-7 REGISTRY RN Entered STN: 14 Jun 2004 EDCN Propanoic acid, 2-hydroxy-, compd. with 4-amino-5-fluoro-3-[6-(4-methyl-1-piperazinyl)-1H-benzimidazol-2-yl]-2(1H)quinolinone (1:1) (CA INDEX NAME) OTHER CA INDEX NAMES: Propanoic acid, 2-hydroxy-, compd. with 4-amino-5-fluoro-3-[5-(4-methyl-1-piperazinyl)-1H-benzimidazol-2-yl]-2(1H)quinolinone (1:1) (9CI) OTHER NAMES: CN CHIR 258 CN Dovitinib lactate TKI 258 CN DR 1000873-96-0 C21 H21 F N6 O . C3 H6 O3 MF SR LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL CM1 CRN 405169-16-6 CMF C21 H21 F N6 O

T.1

L3

L4

CM 2

CRN 50-21-5 CMF C3 H6 O3

## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

- 61 REFERENCES IN FILE CA (1907 TO DATE)
- 2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
- 63 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s 1000873-96-0/dr

'DR' IS NOT A VALID FIELD CODE L5 0 1000873-96-0/DR

0 1000073 30

=> FIL REGISTRY

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.50	22.40
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-1.64

FILE 'REGISTRY' ENTERED AT 16:50:24 ON 02 DEC 2009 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2009 American Chemical Society (ACS)

Property values tagged with IC are from the  ${\tt ZIC/VINITI}$  data file provided by InfoChem.

STRUCTURE FILE UPDATES: 1 DEC 2009 HIGHEST RN 1194901-26-2 DICTIONARY FILE UPDATES: 1 DEC 2009 HIGHEST RN 1194901-26-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 26, 2009.

Please note that search-term pricing does apply when conducting  ${\tt SmartSELECT}$  searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to: http://www.cas.org/support/stngen/stndoc/properties.html => S 1000873-96-0/RN L6 1 1000873-96-0/RN => SET NOTICE 1 DISPLAY NOTICE SET TO 1 U.S. DOLLAR FOR DISPLAY COMMAND SET COMMAND COMPLETED => D L6 SQIDE 1-YOU HAVE REQUESTED DATA FROM 1 ANSWERS - CONTINUE? Y/(N):y THE ESTIMATED COST FOR THIS REQUEST IS 6.85 U.S. DOLLARS DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y) / N: y ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN RN 692737-80-7 REGISTRY Propanoic acid, 2-hydroxy-, compd. with 4-amino-5-fluoro-3-[6-(4-methyl-1-piperazinyl)-1H-benzimidazol-2-yl]-2(1H)quinolinone (1:1) (CA INDEX NAME) OTHER CA INDEX NAMES: Propanoic acid, 2-hydroxy-, compd. with 4-amino-5-fluoro-3-[5-(4-methyl-1-piperazinyl)-1H-benzimidazol-2-yl]-2(1H)quinolinone (1:1) (9CI) OTHER NAMES: CHIR 258 CN Dovitinib lactate CN CN TKI 258 1000873-96-0 DR C21 H21 F N6 O . C3 H6 O3 MFSR LC CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL DT.CA CAplus document type: Conference; Journal; Patent RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses) RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses) RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); USES (Uses) CM 1

CRN 405169-16-6 CMF C21 H21 F N6 O

CM 2

CRN 50-21-5 CMF C3 H6 O3

## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

- 61 REFERENCES IN FILE CA (1907 TO DATE)
- 2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
- 63 REFERENCES IN FILE CAPLUS (1907 TO DATE)

## => SET NOTICE LOGIN DISPLAY

NOTICE SET TO OFF FOR DISPLAY COMMAND SET COMMAND COMPLETED

=>

=> file caplus		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	2.53	24.93
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-1.64

FILE 'CAPLUS' ENTERED AT 16:50:46 ON 02 DEC 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2009 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 2 Dec 2009 VOL 151 ISS 23 FILE LAST UPDATED: 1 Dec 2009 (20091201/ED) REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2009

USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2009

CAplus now includes complete International Patent Classification (IPC) reclassification data for the third quarter of 2009.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 16

L7 63 L6

=> s 17 and ad<20031107 4775475 AD<20031107 (AD<20031107)

2 L7 AND AD<20031107 L8

=> d 18 1-2 ibib abs

ANSWER 1 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:1242789 CAPLUS

143:477969 DOCUMENT NUMBER:

TITLE: Preparation of benzimidazole quinolinones for inhibiting FGFR3 and treating multiple myeloma

Cai, Shaopei; Chou, Joyce; Harwood, Eric; Heise, Carla INVENTOR(S):

C.; Machajewski, Timothy D.; Ryckman, David; Shang,

Xiao; Wiesmann, Marion; Zhu, Shuguang

PATENT ASSIGNEE(S): Chiron Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 239 pp., Cont.-in-part of U.S.

Ser. No. 644,055.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 20050261307	A1	20051124	US 2004-983174		20041105
US 20040092535	A1	20040513	US 2003-644055		20030819 <
US 7470709	В2	20081230			
CN 1692112	A	20051102	CN 2003-824565		20030819 <
US 20050203101	A1	20050915	US 2004-839793		20040505
ZA 2006003598	A	20080430	ZA 2006-3598		20060505
US 20090281100	A1	20091112	US 2008-317493		20081223
US 20090181979	A1	20090716	US 2009-398130		20090304
PRIORITY APPLN. INFO.:			US 2002-405729P	Ρ	20020823
			US 2002-426107P	P	20021113
			US 2002-426226P	Ρ	20021113
			US 2002-426282P	P	20021113
			US 2002-428210P	P	20021121
			US 2003-460327P	P	20030403
			US 2003-460328P	P	20030403
			US 2003-460493P	P	20030403
			US 2003-478916P	P	20030616

US 2003-484048P 20030701 P US 2003-644055 A2 20030819 US 2003-517915P Р 20031107 Ρ US 2003-526425P 20031202 Ρ US 2003-526426P 20031202 Р US 2004-546017P 20040219 US 2004-982543 B1 20041105

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT OTHER SOURCE(S): MARPAT 143:477969

AΒ The title compds. I [A, B, C, and D = C, N; R1-R3 = H, halo, CN, NO2, etc.; R4 = H, alkyl; R5-R8 = H, halo, CN, NO2, etc.; R9 = H, (un) substituted alkyl, aryl, etc.; R10 = H], useful for inhibiting fibroblast growth factor receptor 3 or treating a biol. condition mediated by fibroblast growth factor receptor 3, were prepared E.g., a multi-step synthesis of 4-amino-5-fluoro-3-[6-(4-methylpiperazin-1-yl)-1Hbenzimidazol-2-yl]-1H-quinolin-2-one (II), starting from 5-chloro-2-nitroaniline and 1-methylpiperazine, was given. The majority of the exemplary compds. I displayed an IC50 of less than 10  $\mu M$  with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, Cdk4, MEK1, NEK-2, CHK2, CK1&, Raf, Fyn, Lck, Rsk2, PAR-1, c-Kit, c-ABL, p60src, FGFR3, FLT-3, PDGFR $\alpha$ , and PDGFR $\beta$ . In addition, many of the exemplary compds. exhibited IC50 values in the nM range and show potent activity with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, FGFR3, c-Kit, c-ABL, FLT-3, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, MEK1, CHK2, Fyn, Lck, Rsk2, PAR-1, PDGFR $\alpha$ , and PDGFR $\beta$  with IC50 values of less than 1  $\mu\text{M.}$  The mentioned above compound II was tested in various tests and showed significant antiproliferative activity. II inhibited FGFR3 receptor phosphorylation and ERK phosphorylation in multiple myeloma cell lines with activating FGFR3 mutations.

Ι

OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD (4 CITINGS)

L8 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2005:1223876 CAPLUS

DOCUMENT NUMBER: 143:477966

TITLE: Preparation of benzimidazole quinolinones for

inhibiting a checkpoint kinase 1 and their use in

combination therapy for cancer

INVENTOR(S): Gesner, Thomas G.; Barsanti, Paul A.; Harrison,

Stephen D.; Ni, Zhi-Jie; Brammeier, Nathan M.; Zhou,

Yasheen; Le, Vincent P.

PATENT ASSIGNEE(S): Chiron Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 249 pp., Cont.-in-part of U.S.

Ser. No. 644,055.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
US 20050256157	A1	20051117	US	2005-41191	_	20050121
US 20040092535	A1	20040513	US	2003-644055		20030819 <
US 7470709	В2	20081230				
CN 1692112	A	20051102	CN	2003-824565		20030819 <
US 20050203101	A1	20050915	US	2004-839793		20040505
US 20090281100	A1	20091112	US	2008-317493		20081223
PRIORITY APPLN. INFO.:			US	2002-405729P	P	20020823
			US	2002-426107P	Ρ	20021113
			US	2002-426226P	P	20021113
			US	2002-426282P	Ρ	20021113
			US	2002-428210P	Ρ	20021121
			US	2003-460327P	Ρ	20030403
			US	2003-460328P	Ρ	20030403
			US	2003-460493P	Р	20030403
			US	2003-478916P	Р	20030616
			US	2003-484048P	Р	20030701
			US	2003-644055	_ A2	20030819
			US	2004-538984P	P	20040123

ASSIGNMENT HISTORY FOR US PATENT AVAILABLE IN LSUS DISPLAY FORMAT OTHER SOURCE(S): CASREACT 143:477966; MARPAT 143:477966 GI

Ι

AB The title compds. [I; A, B, C, D = C, N; R1 = H, halo, CN, NO2, etc.; R2, R3 = H, halo, NO2, CN, etc.; R4 = H, (un)substituted alkyl; R5, R8 = H, (un)substituted alkyl, alkenyl, heterocyclyl; or R5 may be absent if A = N; or R8 may be absent if D = N; R6, R7 = H, halo, NO2, CN, etc.; R9 = H, (un)substituted alkyl, aryl, etc.; R10 = H; or R9 and R10 join together to form one or more rings, each having 5-7 members], useful for inhibiting checkpoint kinase 1, inducing cell cycle progression, and increasing

apoptosis in cells, were prepared E.g., a multi-step synthesis of 4-amino-3-(benzimidazol-2-yl)-6-(4-methylpiperazinyl)hydroquinolin-2-one, was given. The compds. I were tested against various kinases. Two of the prepared compds. I, 4-[(3S)-1-azabicyclo[2.2.2]oct-3-ylamino]-3-(1Hbenzimidazol-2-yl)-6-chloroguinolin-2-(1H)-one and 6-chloro-3-[5-(4-methylpiperazin-1-yl)-1H-benzimidazol-2-yl]-4-[(piperidin-2-ylmethyl)amino]quinolin-2(1H)-one, were found to be potent inhibitors of CHK1 with IC50 of 0.32 nM and 0.63 nM, resp. The majority of the exemplary compds. I displayed an IC50 of less than 10  $\mu$ M with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, Cdk4, MEK1, NEK-2, CHK2, CK1ε, Raf, Fyn, Lck, Rsk2, PAR-1, c-Kit, c-ABL, p60src, FGFR3, FLT-3, PDGFR $\alpha$ , and PDGFR $\beta$ . In addition, many of the exemplary compds. exhibited IC50 values in the nM range and show potent activity with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, FGFR3, c-Kit, c-ABL, FLT-3, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, MEK1, CHK2, Fyn, Lck, Rsk2, PAR-1, PDGFR $\alpha$ , and PDGFR $\beta$  with IC50 values of less than 1  $\mu\text{M}$ . The compds. I may be used to prepare pharmaceutical compns. and may be used in conjunction with DNA damaging agents. OS.CITING REF COUNT: 4 THERE ARE 4 CAPLUS RECORDS THAT CITE THIS RECORD

(4 CITINGS)

=> d his

L5

(FILE 'HOME' ENTERED AT 16:47:45 ON 02 DEC 2009)

FILE 'REGISTRY' ENTERED AT 16:47:57 ON 02 DEC 2009

L1 1 S CHIR 258/CN

L2 31 S 405169-16-6/CRN

FILE 'CAPLUS' ENTERED AT 16:49:05 ON 02 DEC 2009

L3 64 S L2

L4 2 S L3 AND AD<20031107

FILE 'REGISTRY' ENTERED AT 16:49:48 ON 02 DEC 2009

FILE 'CAPLUS' ENTERED AT 16:49:49 ON 02 DEC 2009 0 S 1000873-96-0/DR

FILE 'REGISTRY' ENTERED AT 16:50:24 ON 02 DEC 2009

L6 1 S 1000873-96-0/RN
SET NOTICE 1 DISPLAY
SET NOTICE LOGIN DISPLAY

FILE 'CAPLUS' ENTERED AT 16:50:46 ON 02 DEC 2009

L7 63 S L6

L8 2 S L7 AND AD<20031107

=> file medline embase biosis COST IN U.S. DOLLARS

COST IN U.S. DOLLARS
SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST
9.24
34.17

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE
ENTRY
SESSION

CA SUBSCRIBER PRICE

-1.64
-3.28

FILE 'MEDLINE' ENTERED AT 16:51:43 ON 02 DEC 2009

FILE 'EMBASE' ENTERED AT 16:51:43 ON 02 DEC 2009 Copyright (c) 2009 Elsevier B.V. All rights reserved.

FILE 'BIOSIS' ENTERED AT 16:51:43 ON 02 DEC 2009 Copyright (c) 2009 The Thomson Corporation

=> s 12

L9 0 L2

=> s 12<chem>

SmartSELECT INITIATED

New TRANSFER and ANALYZE Commands Now Available See HELP TRANSFER and HELP ANALYZE for Details

COST IN U.S. DOLLARS

SINCE FILE TOTAL
ENTRY SESSION

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

CA SUBSCRIBER PRICE

SINCE FILE TOTAL
ENTRY SESSION

-3.28

FILE 'REGISTRY' ENTERED AT 16:51:51 ON 02 DEC 2009 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2009 American Chemical Society (ACS)

SET SMARTSELECT ON SET COMMAND COMPLETED

SEL L2 1- CHEM

L10 SEL L2 1- CHEM: 36 TERMS

SET SMARTSELECT OFF SET COMMAND COMPLETED

COST IN U.S. DOLLARS

SINCE FILE TOTAL
ENTRY SESSION

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

CA SUBSCRIBER PRICE

SINCE FILE TOTAL
ENTRY SESSION

-3.28

FILE 'MEDLINE' ENTERED AT 16:51:53 ON 02 DEC 2009

FILE 'EMBASE' ENTERED AT 16:51:53 ON 02 DEC 2009 Copyright (c) 2009 Elsevier B.V. All rights reserved.

FILE 'BIOSIS' ENTERED AT 16:51:53 ON 02 DEC 2009 Copyright (c) 2009 The Thomson Corporation

S L10

L11 107 L10

=> s l11 and (?cancer? or ?tumor? or ?tumour? or ?neoplasm?)
L12 93 L11 AND (?CANCER? OR ?TUMOR? OR ?TUMOUR? OR ?NEOPLASM?)

=> dup rem 112

PROCESSING COMPLETED FOR L12

L13 87 DUP REM L12 (6 DUPLICATES REMOVED)

=> s 113 and pd<20031107 1 FILES SEARCHED...

L14 5 L13 AND PD<20031107

=> d 114 1-5 ibib abs

L14 ANSWER 1 OF 5 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights

reserved on STN

ACCESSION NUMBER: 2003481481 EMBASE

TITLE: The impact of anti-angiogenic agents on cancer

therapy.

AUTHOR: Marme, Dieter (correspondence)

CORPORATE SOURCE: Tumor Biology Center, Institute of Molecular Oncology,

Breisacherstrasse 117, 79106 Freiburg, Germany. marme@tumor

bio.uni-freiburg.de

SOURCE: Journal of Cancer Research and Clinical Oncology, (Nov

2003) Vol. 129, No. 11, pp. 607-620.

Refs: 89

ISSN: 0171-5216 CODEN: JCROD7

COUNTRY: Germany

DOCUMENT TYPE: Journal; General Review; (Review)

FILE SEGMENT: 016 Cancer

030 Clinical and Experimental Pharmacology

037 Drug Literature Index 038 Adverse Reactions Titles

LANGUAGE: English

ENTRY DATE: Entered STN: 29 Dec 2003

Last Updated on STN: 29 Dec 2003

L14 ANSWER 2 OF 5 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights

reserved on STN

ACCESSION NUMBER: 2003373828 EMBASE

TITLE: Anti-cancer drug discovery and development

summit.

AUTHOR: Blakey, David C. (correspondence)

CORPORATE SOURCE: AstraZeneca, Alderley Park, Macclesfield, Cheshire SK10

4TF, United Kingdom. david.blakey@astrazeneca.com Expert Opinion on Investigational Drugs, (1 Sep

SOURCE: Expert Opinion on Investigational Drugs, 2003) Vol. 12, No. 9, pp. 1577-1582.

Refs: 15

ISSN: 1354-3784 CODEN: EOIDER

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Conference Article; (Conference paper)

FILE SEGMENT: 016 Cancer

030 Clinical and Experimental Pharmacology

037 Drug Literature Index 038 Adverse Reactions Titles

LANGUAGE: English SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 2 Oct 2003

Last Updated on STN: 2 Oct 2003

AB The 5th Annual Anti-Cancer Drug Discovery and Development Summit brought together an international group of academic and industry scientists to discuss recent therapeutic developments in the field of oncology. The focus of the meeting was novel targeted approaches, i.e., those agents directed against targets that are overexpressed or overactive in tumour cells. It was acknowledged that cytotoxic agents will continue to play a key role in the treatment of cancer and new developments in this area were also discussed. With over 400 anticancer drugs in clinical development and a number of recent registrations, there is great optimism that significant therapeutic advances can be made.

L14 ANSWER 3 OF 5 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights

reserved on STN

ACCESSION NUMBER: 2003363876 EMBASE

TITLE: American Association for Cancer Research - 9th

Annual Meeting: Investigating drugs: 11-14 July 2003,

Washington, DC, USA.

AUTHOR: Mackay, Janie (correspondence); Williams, Laura

CORPORATE SOURCE: Thomson Current Drugs, Middlesex House, 34-42 Cleveland

Street, London W1T 4JE, United Kingdom. laura.williams@curr

ent-drugs.com; janie.mackay@current-drugs.com

SOURCE: IDrugs, (1 Aug 2003) Vol. 6, No. 8, pp. 736-738.

ISSN: 1369-7056 CODEN: IDRUFN

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Conference Article; (Conference paper)

FILE SEGMENT: 016 Cancer

O30 Clinical and Experimental Pharmacology
O36 Health Policy, Economics and Management

037 Drug Literature Index 038 Adverse Reactions Titles

052 Toxicology

LANGUAGE: English

ENTRY DATE: Entered STN: 25 Sep 2003

Last Updated on STN: 25 Sep 2003

L14 ANSWER 4 OF 5 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights

reserved on STN

ACCESSION NUMBER: 2003276961 EMBASE

TITLE: Kinases - SMi Conference 9-10 April 2003, London, UK.

AUTHOR: Harrison, Ruth (correspondence)

CORPORATE SOURCE: Thomson Current Drugs, Middlesex House, 34-42 Cleveland

Street, London W1T 4LB, United Kingdom. ruth.harrison@curre

nt-drugs.com

SOURCE: IDrugs, (1 Jun 2003) Vol. 6, No. 6, pp. 560-562.

ISSN: 1369-7056 CODEN: IDRUFN

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Conference Article; (Conference paper)
FILE SEGMENT: 029 Clinical and Experimental Biochemistry
030 Clinical and Experimental Pharmacology

O31 Arthritis and Rheumatism
O37 Drug Literature Index

LANGUAGE: English SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 24 Jul 2003

Last Updated on STN: 24 Jul 2003

AB Dr. Moss briefly summed up the conference by describing the growth in the development of kinase research over the years and the commitment being invested by companies aiming to find effective screening strategies. He closed the day by remarking on the new challenge for researchers of

turning the concepts discussed into successful drugs.

L14 ANSWER 5 OF 5 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:501918 BIOSIS DOCUMENT NUMBER: PREV200300498316

TITLE: Preclinical pharmacokinetics and metabolism of CHIR258, a

potent tyrosine kinase inhibitor.

AUTHOR(S): Vora, Jayesh [Reprint Author]; Haroldsen, Peter [Reprint

Author]; Renhowe, Paul [Reprint Author]; Heise, Carla [Reprint Author]; Steigerwalt, Ronald [Reprint Author]; Todd, Marque [Reprint Author]; Harris, Alex [Reprint

Author]; Samara, Emil [Reprint Author]

CORPORATE SOURCE: Chiron Corporation, Emeryville, CA, USA

SOURCE: Proceedings of the American Association for Cancer Research

Annual Meeting, (July 2003) Vol. 44, pp. 753.

print.

Meeting Info.: 94th Annual Meeting of the American

Association for Cancer Research. Washington, DC, USA. July

11-14, 2003. ISSN: 0197-016X.

DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 29 Oct 2003

Last Updated on STN: 29 Oct 2003

=> FIL STNGUIDE

COST IN U.S. DOLLARS
SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
SINCE FILE TOTAL

CA SUBSCRIBER PRICE ENTRY SESSION 0.00 -3.28

FILE 'STNGUIDE' ENTERED AT 16:53:40 ON 02 DEC 2009 USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT COPYRIGHT (C) 2009 AMERICAN CHEMICAL SOCIETY (ACS)

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Nov 27, 2009 (20091127/UP).

=> d his

(FILE 'HOME' ENTERED AT 16:47:45 ON 02 DEC 2009)

FILE 'REGISTRY' ENTERED AT 16:47:57 ON 02 DEC 2009

L1 1 S CHIR 258/CN L2 31 S 405169-16-6/CRN

FILE 'CAPLUS' ENTERED AT 16:49:05 ON 02 DEC 2009

L3 64 S L2

L4 2 S L3 AND AD<20031107

FILE 'REGISTRY' ENTERED AT 16:49:48 ON 02 DEC 2009

FILE 'CAPLUS' ENTERED AT 16:49:49 ON 02 DEC 2009 L5 0 S 1000873-96-0/DR

FILE 'REGISTRY' ENTERED AT 16:50:24 ON 02 DEC 2009

L6 1 S 1000873-96-0/RN
SET NOTICE 1 DISPLAY
SET NOTICE LOGIN DISPLAY

FILE 'CAPLUS' ENTERED AT 16:50:46 ON 02 DEC 2009

L7 63 S L6

L8 2 S L7 AND AD<20031107

FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 16:51:43 ON 02 DEC 2009 L9 0 S L2

FILE 'REGISTRY' ENTERED AT 16:51:51 ON 02 DEC 2009 SET SMARTSELECT ON

L10 SEL L2 1- CHEM: 36 TERMS

## SET SMARTSELECT OFF

	FILE	'MEDLINE, E	MBASE,	BIOSIS'	ENTERED	AT 16	:51:53 ON	02	DEC 2009
L11		107 S L10							
L12		93 S L11	AND (	?CANCER?	OR ?TUMC	R? OR	?TUMOUR?	OR	?NEOPLASM?)
т 1 Э		07 DIID D	DM T10	/C DIIDI		MOTTED	. 1		

L13 87 DUP REM L12 (6 DUPLICATES REMOVED) L14 5 S L13 AND PD<20031107

FILE 'STNGUIDE' ENTERED AT 16:53:40 ON 02 DEC 2009

=>

---Logging off of STN---

=>

Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.07	76.20
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-3.28

STN INTERNATIONAL LOGOFF AT 16:54:08 ON 02 DEC 2009